

WHAT IS CLAIMED IS:

1. A composition comprising:

- (a) a non-natural molecular scaffold comprising:
 - (i) a core particle selected from the group consisting of:
 - (1) a core particle of non-natural origin; and
 - (2) a core particle of natural origin; and
 - (ii) an organizer comprising at least one first attachment site, wherein said organizer is connected to said core particle by at least one covalent bond,;
- (b) an antigen or antigenic determinant with at least one second attachment site, wherein said antigen or antigenic determinant is amyloid beta peptide (A β ₁₋₄₂) or a fragment thereof, and wherein said second attachment site being selected from the group consisting of:
 - (i) an attachment site not naturally occurring with said antigen or antigenic determinant; and
 - (ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site; and

wherein said antigen or antigenic determinant and said scaffold interact through said association to form an ordered and repetitive antigen array.

2. The composition of claim 1, wherein said association is by way of at least one covalent bond.

3. The composition of claim 2, wherein said one covalent bond is a non-peptide bond.

4. The composition of claim 2, wherein said one covalent bond is a peptide bond.

5. The composition of claim 1, wherein said core particle is selected from the group consisting of:

- i) a virus;
- ii) a virus-like particle;
- iii) a bacteriophage;
- iv) a bacterial pilus;

20231103-36805002

- v) a viral capsid particle; and
- vi) a recombinant form of (i), (ii), (iii), (iv) or (v).

6. The composition of claim 5, wherein said organizer is a polypeptide or residue thereof and said second attachment site is a polypeptide or residue thereof.

7. The composition of claim 1 or claim 5, wherein said core particle is a virus-like particle.

8. The composition of claim 7, wherein said virus-like particle is a dimer or multimer of a polypeptide comprising amino acids 1-147 of SEQ ID NO:158.

9. The composition of claim 8, wherein said virus-like particle is a dimer or multimer of a polypeptide comprising amino acids 1-152 of SEQ ID NO:158.

10. The composition of claim 9, wherein said first attachment site comprises or is an amino group and said second attachment site comprises or is a sulphydryl group.

11. The composition of claim 7, wherein said virus-like particle is a Hepatitis B virus capsid protein.

12. The composition of claim 11, wherein said first attachment site comprises or is a lysine residue and said second attachment site comprises or is a cysteine residue.

13. The composition of claim 12, wherein one or more cysteine residues of said Hepatitis B virus capsid protein have been either deleted or substituted with another amino acid residue.

14. The composition of claim 12, wherein said Hepatitis B virus capsid protein comprises an amino acid sequence selected from the group consisting of:

- a) the amino acid sequence of SEQ ID NO:89;
- b) the amino acid sequence of SEQ ID NO:90;
- c) the amino acid sequence of SEQ ID NO:93;
- d) the amino acid sequence of SEQ ID NO:98;
- e) the amino acid sequence of SEQ ID NO:99;

2020IT010-8680500T

- f) the amino acid sequence of SEQ ID NO:102;
- g) the amino acid sequence of SEQ ID NO:104;
- h) the amino acid sequence of SEQ ID NO:105;
- i) the amino acid sequence of SEQ ID NO:106;
- j) the amino acid sequence of SEQ ID NO:119;
- k) the amino acid sequence of SEQ ID NO:120;
- l) the amino acid sequence of SEQ ID NO:123;
- m) the amino acid sequence of SEQ ID NO:125;
- n) the amino acid sequence of SEQ ID NO:131;
- o) the amino acid sequence of SEQ ID NO:132;
- p) the amino acid sequence of SEQ ID NO:134;
- q) the amino acid sequence of SEQ ID NO:157; and
- r) the amino acid sequence of SEQ ID NO:158.

15. The composition of claim 14, wherein one or more cysteine residues of said Hepatitis B virus capsid protein have been either deleted or substituted with another amino acid residue.

16. The composition of claim 15, wherein the cysteine residues corresponding to amino acids 48 and 107 in SEQ ID NO:134 have been either deleted or substituted with another amino acid residue.

17. The composition of claim 14, wherein one or more lysine residue of said Hepatitis B virus capsid protein have been either deleted or substituted with another amino acid residue.

18. The composition of claim 1, wherein said core particle is a bacterial pilus.

19. The composition of claim 18, wherein said bacterial pilus is a Type-1 pilus of *Escherichia coli*.

20. The composition of claim 19, wherein pilin subunits of said Type-1 pilus comprises the amino acid sequence shown in SEQ ID NO:146.

21. The composition of claim 1, wherein said core particle comprises a bacterial pilin polypeptide.

22. The composition of claim 21, wherein said bacterial pilin polypeptide comprises the amino acid sequence shown in SEQ ID NO:146.

23. The composition of claim 7, wherein said virus-like particle comprising recombinant proteins, or fragments thereof, being selected from the group consisting of:

- (a) recombinant proteins of Hepatitis B virus;
- (b) recombinant proteins of measles virus;
- (c) recombinant proteins of Sindbis virus;
- (d) recombinant proteins of Rotavirus;
- (e) recombinant proteins of Foot-and-Mouth-Disease virus;
- (f) recombinant proteins of Retrovirus;
- (g) recombinant proteins of Norwalk virus;
- (h) recombinant proteins of Alphavirus;
- (i) recombinant proteins of human Papilloma virus;
- (j) recombinant proteins of Polyoma virus;
- (k) recombinant proteins of bacteriophages; and
- (l) recombinant proteins of RNA-phages;
- (m) recombinant proteins of Q β -phage;
- (n) recombinant proteins of GA-phage
- (o) recombinant proteins of fr-phage; and
- (p) recombinant proteins of Ty.

24. The composition of claim 7, wherein said virus-like particle comprising, or alternatively essentially consisting of, recombinant proteins, or fragments thereof, of a RNA-phage.

25. The composition of claim 7, wherein said virus-like particle comprising, or alternatively essentially consisting of, recombinant proteins, or fragments thereof, of a RNA-phage being selected from the group consisting of:

- a) bacteriophage Q β ;
- b) bacteriophage R17;
- c) bacteriophage fr;
- d) bacteriophage GA;
- e) bacteriophage SP;
- f) bacteriophage MS2;

203710-660502

203740-66805007

- g) bacteriophage M11;
- h) bacteriophage MX1;
- i) bacteriophage NL95;
- k) bacteriophage f2; and
- l) bacteriophage PP7.

26. The composition of claim 7, wherein said virus-like particle comprising, or alternatively essentially consisting of, recombinant proteins, or fragments thereof, of bacteriophage Q β

27. The composition of claim 7, wherein said virus-like particle comprising, or alternatively essentially consisting of, recombinant proteins, or fragments thereof, of bacteriophage fr.

28. The composition of claim 1, wherein said core particle is selected from the group consisting of:

- i) a virus-like particle;
- ii) a bacterial pilus; and
- iii) a virus-like particle of a RNA-phage.

29. The composition of claim 7,11,14,18,24-27, wherein said second attachment site does not naturally occur within said antigen or antigenic determinant.

30. The composition of claim 29, wherein said composition comprises an amino acid linker.

31. The composition of claim 30, wherein said amino acid linker is bound to said antigen or said antigenic determinant by way of at least one covalent bond.

32. The composition of claim 31, wherein said covalent bond is a peptide bond.

33. The composition of 30, wherein said amino acid linker comprises, or alternatively consist of, said second attachment site.

34. The composition of claim 33, wherein said amino acid linker comprises a sulphydryl group or a cysteine residue.

35. The composition of claim 33, wherein said amino acid linker is selected from the group consisting of:

- (a) CGG
- (b) N-terminal gamma 1-linker;
- (c) N-terminal gamma 3-linker;
- (d) Ig hinge regions;
- (e) N-terminal glycine linkers;
- (f) $(G)_nC(G)_k$ with $n=0-12$ and $k=0-5$;
- (g) N-terminal glycine-serine linkers
- (h) $(G)_kC(G)_m(S)(GGGGS)_l$ with $n=0-3$, $k=0-5$, $m=0-10$, $l=0-2$;
- (i) GGC
- (k) GGC-NH₂
- (l) C-terminal gamma 1-linker
- (m) C-terminal gamma 3-linker
- (n) C-terminal glycine linkers
- (o) $(G)_nC(G)_k$ with $n=0-12$ and $k=0-5$;
- (p) C-terminal glycine-serine linkers
- (q) $(G)_m(S)_l(GGGGS)_n(G)_oC(G)_k$ with $n=0-3$, $k=0-5$, $m=0-10$, $l=0-2$, and $o=0-8$.

36. The composition of claim 1, wherein said amyloid beta peptide (A β ₁₋₄₂) or a fragment thereof is selected from the group consisting of:

- a) A β 1-15;
- b) A β 1-27;
- c) A β 1-40;
- d) A β 1-42;
- e) A β 33-40; and
- e) A β 33-42.

202503994-04-02

37. The composition of claim 36 further comprising a heterobifunctional cross-linker, preferably selected from the group consisting of:

- a) SMPH;
- b) Sulfo-MBS;
- c) Sulfo-GMBS

38. The composition of claim 1, wherein said amyloid beta peptide (AB₁₋₄₂) or fragment thereof with said second attachment site has an amino acid sequence selected from the group consisting of:

- a) the amino acid sequence of DAEFRHDSGYEVHHQGGC;
- b) the amino acid sequence of CGHGNKSGLMVGGVIA; and
- c) the amino acid sequence of
DAEFRHDSGYEVHHQKLVFFAEDVGSNGC.

39. The composition of claim 38, wherein said core particle is selected from the group consisting of:

- a) a virus-like particle comprising, alternatively consisting of, recombinant proteins, or fragments thereof of bacteriophage Q β ;
- b) a virus-like particle comprising, alternatively consisting of, recombinant proteins, or fragments thereof of bacteriophage fr;
- c) a virus-like particle of HBcAg-lys-2cys-Mut;
- d) a bacterial pilus; and
- e) a Type-1 pilus of *Escherichia coli*.

40. The composition of claim 36, wherein said first attachment site comprises or is an amino group and said second attachment site comprises or is a sulphydryl group.

41. The composition of claim 36, wherein said first attachment site comprises or is a lysine residue and said second attachment site comprises or is a cysteine residue.

42. The composition of claim 36, wherein said second attachment site does not naturally occur within said antigen or antigenic determinant.

43. The composition of claim 42, wherein said composition comprises an amino acid linker.

208170-86805001

44. The composition of claim 43, wherein said amino acid linker is bound to said antigen or said antigenic determinant by way of at least one covalent bond.

45. The composition of claim 43, wherein said covalent bond is a peptide bond.

46. The composition of 43, wherein said amino acid linker comprises, or alternatively consist of, said second attachment site.

47. The composition of claim 46, wherein said amino acid linker comprises a sulphydryl group or a cysteine residue.

48. The composition of claim 36 or 46, wherein said amino acid linker is selected from the group consisting of:

- (a) CGG
- (b) N-terminal gamma 1-linker;
- (c) N-terminal gamma 3-linker;
- (d) Ig hinge regions;
- (e) N-terminal glycine linkers;
- (f) $(G)_k C(G)_n$ with $n=0-12$ and $k=0-5$;
- (g) N-terminal glycine-serine linkers
- (h) $(G)_k C(G)_m(S)_l(GGGGS)_n$ with $n=0-3$, $k=0-5$, $m=0-10$, $l=0-2$;
- (i) GGC
- (k) GGC-NH2, GGC-NMe, GGC-N(Me)2, GGC-NHET or GGC-N(Et)2;
- (l) C-terminal gamma 1-linker
- (m) C-terminal gamma 3-linker
- (n) C-terminal glycine linkers
- (o) $(G)_n C(G)_k$ with $n=0-12$ and $k=0-5$;
- (p) C-terminal glycine-serine linkers
- (q) $(G)_m(S)_l(GGGGS)_n(G)_o C(G)_k$ with $n=0-3$, $k=0-5$, $m=0-10$, $l=0-2$, and $o=0-8$.

49. The composition of claim 36, wherein said amino acid linker is selected from the group consisting of:

20231010868050014

- (a) CGG
- (b) CGKR;
- (c) CGHGNKS;
- (d) GGC;
- (e) GGC-NH2;

50. A pharmaceutical composition comprising:
a) the composition of claim 1; and
b) an acceptable pharmaceutical carrier.

51. A method of immunization comprising administering the composition of claim 1 to a subject.

52. A vaccine composition comprising the composition of claim 1.

53. A process for producing a non-naturally occurring, ordered and repetitive antigen array comprising:

- a) providing a non-natural molecular scaffold comprising:
 - (i) a core particle selected from the group consisting of:
 - (1) a core particle of non-natural origin; and
 - (2) a core particle of natural origin; and
 - (ii) an organizer comprising at least one first attachment site, wherein said organizer is connected to said core particle by at least one covalent bond; and
- b) providing an antigen or antigenic determinant with at least one second attachment site, wherein said antigen or antigenic determinant is amyloid beta peptide (A β ₁₋₄₂) or a fragment thereof, and wherein said second attachment site being selected from the group consisting of:
 - (i) an attachment site not naturally occurring with said antigen or antigenic determinant; and
 - (ii) an attachment site naturally occurring with said antigen or antigenic determinant,

wherein said second attachment site is capable of association through at least one non-peptide bond to said first attachment site; and

- c) combining said non-natural molecular scaffold and said antigen or antigenic determinant,

wherein said antigen or antigenic determinant and said scaffold interact through said association to form an ordered and repetitive antigen array.